

DETAILED ACTION

Receipt of applicants' amendments and remarks submitted January 9, 2008 is acknowledged.

Claim Rejections 35 U.S.A. 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. Claims 1-3, 6-7, 13-15, 18-19, 32-34, 37-38, 44-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Waldinger et al. (NL 1012954, and Maturitas, 2000, vol. 36, pages 165-168), in further view of Andrews et al. (WO 01/52855).

3. Waldinger et al. teaches a method of treating patients suffering hot flushing and perspiration with mirtazapine. See, the abstract of NL 1012954 and Maturitas. Waldinger et al. discloses that mirtazapine is particularly effective in alleviating perspiration. See, particularly the cases in Maturitas.

4. Waldinger et al. do not teach expressly the treatment of primary hyperhidrosis or idiopathic hyperhidrosis, or the particular dosage form of mirtazapine.

However, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to treat idiopathic hyperhidrosis patients with mirtazapine for alleviating perspiration.

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A person of ordinary skill in the art would have been motivated treat idiopathic hyperhidrosis patients for alleviating perspiration with mirtazapine because mirtazapine is known to be useful in alleviating perspiration. One of ordinary skill in the art would have reasonably expected that mirtazapine would be symptomatically useful for treating perspiration caused by any etiologies as it has been shown that mirtazapine is particularly effective in alleviating perspiration. Further, Andrews reveals that mirtazapine is an old and well-known therapeutical agent and may be formulated to conventional dosage forms for oral, parenteral, topical administrations. See, particularly, page 1, lines 16-19, page 8, line 4-38. Therefore, making a particular dosage form, such as liposome, or selecting a particular administration method for mirtazapine would have been within the purview of ordinary skill in the art. Finally, it is noted that perspiration for patient with hyperhidrosis happens periodically, the treatment as disclosed by Waldinger et al. do not require the administration be carried out at the time of perspiration, therefore, would meet the limitation “prophylactically” recited in claims 32.

Claims 1-3, 6-7, 13-15, 18-19, 32-34, 37-38, 44-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Waldinger et al. (NL 1012954, and Maturitas, 2000, vol. 36, pages 165-168), in view of Davidson et al. (IDS), and in further view of Andrews et al. (WO 01/52855).

5. Waldinger et al. teaches a method of treating patients suffering hot flushing and perspiration with mirtazapine, a serotonin antagonist. See, the abstract of NL 1012954 and Maturitas. Waldinger et al. discloses that mirtazapine is particularly effective in alleviating perspiration. See, particularly the cases in Maturitas.

6. Waldinger et al. do not teach expressly the treatment of primary hyperhidrosis or idiopathic hyperhidrosis.

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However, Davidson teaches that fluoxetine an antidepressant and serotonin antagonist is effective for reduce the symptoms of hyperhidrosis in patients of social anxiety disorders and suggest serotonergic mechanism is associated with the hyperhidrosis. See, particularly, the abstract at page 1327, and the discussion and conclusion at pages 1330-1331.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to treat idiopathic hyperhidrosis patients with serotonin antagonist, such as mirtazapine for alleviating perspiration.

A person of ordinary skill in the art would have been motivated to treat idiopathic hyperhidrosis patients for alleviating perspiration with mirtazapine because serotonin antagonists, mirtazapine in particular, are known to be useful in alleviating perspiration. One of ordinary skill in the art would have reasonably expected that mirtazapine would be symptomatically useful for treating perspiration caused by any etiologies as it has been shown that mirtazapine is particularly effective in alleviating perspiration. Further, Andrews reveals that mirtazapine is an old and well-known therapeutical agent and may be formulated to conventional dosage forms for oral, parenteral, topical administrations. See, particularly, page 1, lines 16-19, page 8, line 4-38. Therefore, making a particular dosage form, such as liposome, or selecting a particular administration method for mirtazapine would have been within the purview of ordinary skill in the art. Finally, it is noted that perspiration for patient with hyperhidrosis happens periodically, the treatment as disclosed by Waldinger et al. do not require the administration be carried out at the time of perspiration, therefore, would meet the limitation “prophylactically” recited in claims 32.

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7. Claims 11, 12, 23, 24, 42, and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Waldinger et al. (NL 1012954, and Maturitas, 2000, vol. 36, pages 165-168), in further view of Andrews et al. (WO 01/52855) for reasons discussed above, and in further view of Saadia et al. (IDS).

Waldinger et al. and Andrews as a whole do not teach expressly the further injection of botulinum.

However, Saadia et al. teaches that local intradermal injection of botulinum is known to be useful for treating hyperhidrosis.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to further incorporate a step of injection botulinum for treatment of hyperhidrosis.

A person of ordinary skill in the art would have been motivated to further incorporate a step of injection botulinum for treatment of hyperhidrosis because it is prima facie obvious to combine two compositions each of which is taught in the prior art to be useful for same purpose in order to form third composition (or method of using the same) that is to be used for very the same purpose; idea of combining them flows logically from their having been individually taught in prior art; See In re Kerkhoven, 205 USPQ 1069.

8. Claims 11, 12, 23, 24, 42, and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Waldinger et al. (NL 1012954, and Maturitas, 2000, vol. 36, pages 165-168), in view of Davidson et al. (IDS), and in further view of Andrews et al. (WO 01/52855) for reasons discussed above, and in further view of Saadia et al. (IDS).

Waldinger et al. Davidson et al. and Andrews as a whole do not teach expressly the further injection of botulinum.

However, Saadia et al. teaches that local intradermal injection of botulinum is known to be useful for treating hyperhidrosis.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to further incorporate a step of injection botulinum for treatment of hyperhidrosis.

A person of ordinary skill in the art would have been motivated to further incorporate a step of injection botulinum for treatment of hyperhidrosis because it is prima facie obvious to combine two compositions each of which is taught in the prior art to be useful for same purpose in order to form third composition (or method of using the same) that is to be used for very the same purpose; idea of combining them flows logically from their having been individually taught in prior art; See In re Kerkhoven, 205 USPQ 1069.

Response to the Arguments

Applicants' amendments and remarks submitted January 9, 2008 have been fully considered. The amendments and remarks are persuasive to overcome the rejections under 35 U.S.C. 102, but are not persuasive as to the rejections set forth above.

9. With respect to the rejection under 35 U.S.C. 103 over Waldinger et al. in view of Andrews et al. (WO 01/52855), applicants contend that skilled artisan would have not expected mirtazapine be useful in treatment of perspiration by other etiologies because Waldinger teach mirtazapine for treatment of hot flash only. The arguments are not persuasive. Applicants' attention is directed to the abstract of Waldinger (Maturitas, or Waldinger II), where it states:

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Conclusion: Mirtazapine appears to have a substantial ameliorating effect on hot flushes *and perspiration bouts*. It is postulated that the 5-HT_{2A} blocking properties of mirtazapine is accounted in the symptomatic relief of hot flushes. In addition it is hypothesized that the serotonergic system is crucially involved in the pathogenesis of hot flushes *and perspiration bouts*. (emphasis added).

It is clear to an ordinary skill in the art that Mirtazapine is useful for symptomatically release of perspiration.

With respect to the rejection under 35 U.S.C. 103 over Waldinger et al. in view of Davidson et al. (IDS), and in further view of Andrews et al. (WO 01/52855), applicants argue that Davidson reference fails to teach method for treating idiopathic hyperhidrosis. It is noted that Davidson teaches that fluoxetine an antidepressant and serotonin antagonist is effective for reduce the symptoms of hyperhidrosis in patients of social anxiety disorders and suggest serotonergic mechanism is associated with the hyperhidrosis. Therefore, considering the cited references as a whole, it would have been obvious to use mirtazapine, a well-known serotonin antagonist, for treatment of hyperhidrosis.

10. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). In instant case, it is known that mirtazapine, a known serotonin antagonist, is useful for symptomatically release of perspiration (hyperhidrosis), and serotonin antagonists have been suggested to be useful for treatment of social anxiety and associated

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idiopathic hyperhidrosis. Based on those knowledge, one of ordinary skill in the art would have been motivated to use mirtazapine for treatments of idiopathic hyperhidrosis.

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shengjun Wang whose telephone number is (571) 272-0632. The examiner can normally be reached on Monday to Friday from 7:00 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

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system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Shengjun Wang/
Primary Examiner, Art Unit 1617